THE RECOVERY KERNEL

Neuroscience Reference Series.

ΔFosB

MUKATI WECHIMWE.

Maitiro, Geneti, Kutarisa, uye Nguva Yokubviswa — Chigadzirwa Chechipiri.

⚠ CHIZVAKO CHEKUDZIDZISA NECHEDZERA KWEKUCHENESA - HAAISI KUNYANGADZO YEMWEDZI KANA YEKUTSVAGISA DZEMAGENETICS.

Nguva yekedemhadaro: fona 994 kana utenge findahelpline.com.

Chinyorwa Chiri Pazera.

Iri ndiro edhini rekubatsirwa, yakawedzwa uye yakawedzera mashoko akajeka nezve nzira dzinobva mumatomu, hutano hwevanhu hunobva pazvidzidzo zvegeneti zvehunyanzvi (kunyange zvazvo izvi hadzisi zvido zvegeneti zvinonyanya kushandiswa), chikamu nezvezvinhu DNA uye zvidzidzo zveepigenetiki zvinogona uye zvinogona kushandiswa, uye mibvunzo mbiri inonyanya kubvunzwa mumagumo ekubudirira: nei kushandiswa kwezvidhori zvakawanda kunonyanya kuita kuti kuuya kumamiriro akangodaro kunge kwakaoma, uye nei kufamba uchidaro panguva yakagadzirirwa kunenge kuchangobva nekugadzwa, uye kunenge kuchangobva nekugadzwa.

ΔFosB haisagona zvakamboverwa zvakananga mumutsivo wevanhu. Zvinhu zvose nezvekukwira uye kudonha kwazvo zvinobva kuzvidzidzo zvemurimuka, kuedza kwekutungamirira jeni nevirasi, uye kuongorora mwezi wevanhu vakaenda. Nguva dzevanhu pano ndezvekufungira, uye zvinoratidzirwa zvakajeka. Kana chigadzirwa ichi chichinetsa kunyatsotenda kupfuura chigadzirwa chepakare, ndekuti sayenzi yacho yakanyatsogadzirirwa, kwete kuti kusava nechokwadi kwapera.

Mubvunzo.

Maitiro ekushandiswa kwezviratidzo zvakafanana anogashirwa pano, sezvakaita mucompendium yese yeRecovery Kernel.

- AKAMIRIRWA — hunhu hwakakajirwa, hunhu hunogumiswa, kuzvimiririra kwevanhu (kazhinji hunhu hunogumiswa mumamiriro ekushandiswa kwezvimwe zviyero, kunyanya ΔFosB; hunhu hunogumiswa kwevanhu hunoratidzirwa kana painenge pachiitiko).
- ZVINOKONZWA — data inofananidzira, zvakakosha kana zvakaratidzwa nemaitiro kana kuferefekwa, uye zvinoratidza kuti zvinotevera imwe pfungwa.
- INOKUJEKA - inogona kuita, iri pachinzvimbo yekutanga, asi kusati kwabva kuenderana.
- AUTHOR/SYSTEM EXPERIENCE — chiyero chinoshandiswa mumaitiro ekubatanidzwa kwefuremu iri; chengetai se hypothesis, kwete chokwadi.
- CONTROVERSIAL/MIXED — active disagreement in the literature.
- ISINAITWA — inyango vanenge vabvunza, asi haisati yakanamirwa zvakajairwa.

1. ΔFosB chaiito cha— nzira, zvakakwana.

[AKAMBO] (mimodhiri yemhando dzemhuka; iyi nzira yakazivikaniswa zvakadzidzisa mumabhuku ezvimiririro zvehutano uye sayenzi hwehutano hwehutano, uye inoshandiswa nevaenzi veEric Nestler).

ΔFosB ndiro yechimiro cheFOSB, uye inoshanda semutsvakurudzi wekutema, - protein inodaro zvinogona kuvhurwa kana kuvharwa kwezvimiro zhinji - inonyanya kuve mu nucleus accumbens, dorsal striatum, uye hippocampal dentate gyrus. Chikonzero nderokuti inowedzera pachayo panzvimbo pekushanduka mushure yemwedzi yega yekuita, ndeyemaitiro maviri ekemikari anoshanda pamwechete:

- Kusungirira kwezvinangwa kunonetsa musuwo wekubuda. Paunenge uchikwikwidzwa zvakawanda, hutano hunotumira mashoko (huchidzorera dopamine D1 receptor, Activin/ALK4 pathway, uye SMAD3–PCBP1 protein complex) hunogona kukanganisa kusungirira kweFOSB pre-mRNA, zvinoita kuti isungirwe zvakasiyana neiyo yakaunganidzwa zvakajairika. Protein yeΔFosB inogadzirwa, uye inenge isina chikamu chekumusoro (C-terminal region) chinenge chiri pachikamu cheFosB yese, chinenge chiri chinhu chinenge chiri kushandiswa kuti protein iyi iwedzerwe nekukurumwa nekukurumwa neubiquitin-proteasome system. Pasina chikamu ichocho, ΔFosB inogara kwenguva refu kupfuura protein yacho yega, asi inenge ichiri nyore kuwedzerwa nekukurumwa.
- Phosphorylation inobva nechinzvimbo. Casein Kinase 2 (CK2), enzyme inogara ichishanda mumagadzirirwo emwoyo, inoisa guru rematombo pachinzvimbo chaiyo — Serine 27 — padyo nechinzvimbo rekutanga remapuroteni eΔFosB. Izvi zvinogadzirisa chimiro chemapuroteni, zvinoita kuti asavanzwe zvimwe zvinenge zvaishandisa kuti adzingwe. Iri fomu rakagadziridzwa nderi yakasimba, ye35–37 kDa, iyo inowedzera nekushandiswa kwezvinodhaka kazhinji uye inoramba iri kwenguva refu, kunyange apo kushandiswa kamwe chete kwaizokonzera kuti idzingwe.

Tebhuru iri pazasi inoratidza kusiyana kwazvo izvi anodaro.

Isoform.	Masiya.	Chii chinogona kuita kuti zvive kudaro.	Ngariswa.	Kugara.
Full-length FosB.	~50 kDa	Inochengeta zvikuru zvitatu zvekupera kwepepuroni.	Kubatidzwa kweC-terminal degrons neubiquitin-proteasome zvakananga.	Dzemwedzura — maawa
ΔFosB isina phosphorylation.	~33 kDa	Kuenzanisa kwezviratidzo panzvimbo yekutanga kweexon-4 uye yekupinda kweintron-4 kunobvisa zviratidzo zvekuita kuti zvirege, asi Ser27 inoramba isina kuchengetedzwa.	Kuparadzwa kweiyi protini neprotheasomu nekuda kwezvinogona kuita zvinhu zviri pachinzvimbo cheN-terminal.	Maawa mashoma kusvika zuva rimwe.
Phosphorylated ("yakasimba") ΔFosB.	~35–37 kDa	Casein Kinase 2 (CK2) inogadzirisa Ser27, uye izvi zvinogadzira shanduko pachinhu chemupiro inokanganisa nzira dzinoramba dzichidikanwa dzekuparadzwa.	Inokanzwa kushandiswa nepfungwa yekudzikisira mapuroteni apo ari muenzvimbo yakaderera uye akanyatsofemerwa.	Inogara — inogara mumuviri uye inowedzera kwemwedzi, inogona kuonekwa kwemwedzi kana kusvika kwemwedzi miviri mushure mokunge kuiswa kwadaro

Isoform.	Masiya.	Chii chinogona kuita kuti zvive kudaro.	Ngariswa.	Kugara.
				kwadaro kwedenderedzwa.

Mugumisiro: ΔFosB haidzorwi nekuti inoramba ichidikanwa - mRNA transcription inodarika zvakanyanya apo kushandiswa kweiyi chinhu kwapera. Inodzorwa nekuti, apo yava phosphorylation, inenge isiri nyore kudzorwa. Kudzorwa, pane zvakanyanya, inzwi rekuti tirambe kusvika protein iyi yadzikira, iyi protein yakagadzirirwa kuti isadzikiswi nyore.

2. Kudzidza kweΔFosB mune zvikuru zveRecovery Kernel.

"Relative induction" inongoronga simba reiyi chiitiko, kuita kwakangoita, uye huwandu hwekutanga zvakawanda - matatu mazuva ayo anowanzo kudyidzana nemaitiro emhando yekuzvarwa uye kuita kuti ΔFosB ikwanise kuunganidzwa.

Zvinangwa / Zviito	Maitiro ekuyambisa kuwedzera kweΔFosB.	Induction yechisimbiso.	Mubvunzo.
Mufirimu.	Kuderera kweGABA/glutamate pamwe nekuderera kwe dopamine nekuda kwekushandiswa kazhinji.	Yakatenderera-yakaderera (zvinoenderana ne dosage uye mararamiro).	AKAMBIRWA
Cocaine.	Kudzivirira zvakananga kwekushandiswa kweDAT; kuwanda kwakakura uye nekukurumwa kwe dopamine.	High.	AKAMBIRWA
Crack cocaine	Iyo, inoshanda zvakafanana nekokaini, uye inounzwa mhedzisiro mukati memasekondi 8 apo uchidhumira.	Inokoma zvikuru — kushanda kwakadzika kunotanga nekukurumidza, kunoita kuti kuita zvimwe zvinhu kurongeke nekukurumidza.	AKAMBIRWA
Methamphetamine	DAT/NET reversal - kuburitsa dopamine, kwete kungodereda kuiswa mune.	Zvakakwirira zvikuru.	AKAMBIRWA
MDMA	Kudonha kwakawanda kwe serotonin uye kudonha kwepamusoro kwe dopamine.	Inokwirira (kunonoka kwehutano hwehutano hwe serotonin kunogumisa huwandu hwekushandisa zvakare).	Zvichiri kuposible.
Nicotine.	Kuderera kwezviratidzo zvinonyanya kushandiswa zvinokonzera kufungira	Kureba kwepamusoro	AKAMBIRWA

Zvinangwa / Zviito	Maitiro ekuyambisa kuwedzera kweΔFosB.	Induction yechisimbiso.	Mubvunzo.
	kazhinji (10–20 nguva pazuva).	kunobatsira kushandiswa kwepedyo-pedyo kweiyi mvura.	
Heroin / mishonga inofuridzirwa nemidziyo.	Mu-opioid receptor activation inodereda neuron dhorimaini yeVTA.	Moderate–High	AKAMBIRWA
Fentanyl	Iyo, inoteverawo nzira imwechete neheroini, asi inonyanya kusimba uye inoshanda nekukurumidza.	High.	Zvichiri kuposible.
Benzodiazepines.	GABA-A potentiation; kushandiswa kwe-dopamine kwechipamhenyu.	Diki – Nyakawanda	KUCHENESA.
Marijana (THC)	CB1 activation inodereda neuron dhorimaini dzeVTA.	Diki - Nyakawanda.	KUCHENESA.
Ketamine.	NMDA antagonism; mhedzo we dopamine haungamiriri seiyiwo nemidziyo inosimudza.	Diki – Nyakawanda	KUCHENESA.
GHB.	GABA-B agonism; mhedziso yedopamine inenge yakasiyana uye inenge yakawanda.	Diki – Nyakawanda	KUCHENESA.
Kratom.	Kushandiswa kwezvidhori zvemushonga ane simba rekubatsira, asi anenge achishandisawo zvimwe zvinoshandiswa nemushonga, anogona kuita kuti zvinhu zviite zvakasiyana kana zvakashandiswa zvakawanda.	Pano kusvika pakareba (zvinoenderana nehuwandu).	KUCHENESA.
Mephedrone (4-MMC)	Chidiki chinobvisa zvinhu zvakafanana neDAT, NET, uye SERT, chakafanana nekokaini asi chinogara kwenguva pfupi.	High - hupeny hure hupfupi hunoreva kufanira kushandiswa kazhinji.	KUCHENESA.
Methedrone (bk-PMMA / 4-MeO-methcathinone)	Inenge yakafanana ne-mephedrone; inokonzera kushanda zvakanyanya kune SERT, asi inenge isina simba pakushanda kune DAT.	Inonzwa kunonzi "moderate–high" - inenge ine simba pasi kupfuura mephedrone, asi kufa zvakawanda kungangodaro.	Zvakangoitwa nezvakatangwa nezvinogona kukonzera zvinhu zvakaita sezvinogona kukonzera.
Magadziri / mitambo / mamwe mafomu ekuyerera.	Mubvondo wemamiriro akaita zvakafanana, unoshandiswa nemamiriro ekudzoka-dzoka anenge ashandiswa, panzvimbo yemwedzi.	Zvidiki zvekudzoka kuita basa, asi zvine kushanda kazhinji.	AKAMISIKIDZWA (mabviro, midziyo yekubatsira).
Zvakudya zvine	Kudya zvakawanda zvine sukari	Moderate	Zvichiri kuposible.

Zvinangwa / Zviito	Maitiro ekuyambisa kuwedzera kweΔFosB.	Induction yechisimbiso.	Mubvunzo.
kuravira kwakakura / sukari.	yakawanda uye mafuta akawanda, kazhinji kazhinji, inoratidza zvimwe zvizvo zvinonzi "accumbens ΔFosB signature" sezvakaratidzwa mune zvakawanda zvekutsvakurudza nezvakatsetanzwa.		

Methedrone haisati yasangana nechidzidzo chakafanira kuti ichionekane kuti inokonzera kuwanda kweΔFosB; ruzivo rwacho rwakatangwa nekuti inowanikwa muchikwata checathinone, asi risiri kubva pazvakaratidzwa zvakananga.

3. Mitemo yekubvisa zvinhu - Zvaanoratidza data.

Nguva yekupora kweΔFosB haisati yanyatso cherechedzwa mumunhu ari mupenyu. Nguva dzese dzinotevera dzinobva mumitsetse yenyama yenyama kana kuzvidzidzo shoma zvevanhu vakafa. Chengeta izvi semapurogiramu ekuyerera mabviro, asi usati uishandise semusuwero wekuzvipira kwako.

Zvinoreva chikamu.	Zvinetsa kuti zvinetsa.	Nguva yenguva.	Mubvunzo.
Kukura kwakadzika.	ΔFosB isina phosphorylation inoratidzwa mushure kwekutanga chete; inopisa kwakadzika, uye inokoromoka zvakawanda.	Maawa kusvika zuva rimwe.	AKAMBIRWA
Kuisirwa.	Kukwanidza kazhinji kunogadzira ΔFosB, iyo yakagadzirwa neCK2-phosphorylation, uye isina degron, iyo inokunda kuburitswa neproteasome uye inoramba iri.	Inogadzirwa mazuva nemwedzi nekushandiswa kazhinji.	AKAMBIRWA
Kudzika kwepamusoro.	Kudzidzira kwekuramba kunowedzera kuita kuti zvinhu zvakagadzirwa zviwedzere nekukurumwa, asi kunyange zvakadaro, zvinhu izvo zviri kuwedzera zvinenge zvakanyanya kupfuura nezvinhu zvinoitwa kuti zviwedzere.	Mweduro wevhiki 2-4 kana zvakawanda, uye inogona kushanda zvakanyanya kana iine dosage yakakura kana kushandiswa kazhinji.	INGANGO (yechitarisa, inoshanda zvinoendera na nemitsetse).
Kudzingiswa kwe-mRNA pashure kwekushandiswa kwake kwezuva.	New FOSB inoratidzika zvakaderera mazuva mashoma ekupedzisira, uye hapana protini itsva inogadzirwa.	~24–48 maawa	INGAVO.
Kuderera kwezvimiro.	ΔFosB inogara zvakaoma mumusoro we"nucleus accumbens" uye mumusoro we"striatum", kunyange kana transcription yatadza.	Mwedzi mumwe kusvika mwedzi miviri mune zvakaitwa nemhendere; inogona kuonekwa mumitambo yevarume	ZVINOKANIKA (mukanwa wechimusika + kuongororwa kwevakadzi vashoma pashure kurema).

Zvinoreva chikamu.	Zvinetsa kuti zvinetsa.	Nguva yenguva.	Mubvunzo.
		vakaenda pasi mashanu ezuva, izvo zvinoratidza kuchena kwazvo.	
Kugara kweiyi simbi uye zvinhu zviri mukati.	Shanduko dzemukati medendriti uye kushanduka kwechromatin (ona chikamu che4) inogara kwenguva refu, kunyange apo protein yacho yaderera.	Inogona kuwedzera kwemwedzi kupfuura kuenzaniso yekukura kweΔFosB mumamiriro ekushandiswa kwezvimiro zvehupenyu.	KUCHENESA.

Chokwadi, kupera kweΔFosB protein inenge chakanyanya kunonetsa mwedzi yekutanga apo munhu abva kushandisa chinhu. Asi - uye iyi ndiyo chikamu chakakosha kwazvo chakazvimiririra mumamiriro ezvinhu - kupera kweiyo protein hakusi zvakafanana nekudzorerwa kweiyo circuit. Uku kusiyana ndiyo nyaya yechikamu chinotevera, uye inonyanya kukosha kupfuura zvimwe zvinhu zvinhu zviri muvhaya iri.

4. Chromatin inokwana protein.

[AKAMBO] (mimodhiri yemhando dzemhuka)

Pamusoro pezvo, apo ΔFosB iri kushanda, haisiri kungoramba iri mumatombo—inoshandisa michina yekuchinja chromatin kuenda kumagadziridzo akasiyana-siyana, uye michina iyi inosiiwa nemakaki anogara kwenguva refu, kunyange apo ΔFosB yasvika.

- Pazvo dzinogona kuderedzwa — senge c-fos — ΔFosB inoona nzvimbo dzeAP-1 pane promoter uye inoita kuti Histone Deacetylase 1 (HDAC1) iwane. HDAC1 inobvisa magirafu eacetyl kubva kumakumbo emamiroro ehistone (H3K9), zvinoita kuti iyo DNA yacho iwedzere uye iite heterochromatin. Gene inoita kuti kuita kuti gene yacho iwedzere kuita basa zvive zvakaoma — kuwedzerwa kwakadaro kunoramba zvakakosha kunyange apo protein yeΔFosB yacho yava kupera.
- Pazvo dzinogona kusimbisa — kusanganisira CDK5, subunit yeAMPA receptor inonzi GluA2 (GRIA2), uye ARC — ΔFosB inoda BRG1, iyo subunit huru yeSWI/SNF chromatin-remodeling complex. BRG1 inovhura chromatin panzvimbo idzi, uye mhedzisiro inozvishandura inosanganisira kuwanda kwe dendritic spines panzvimbo dze neurons dziri mu circuit yekubatsira.

Iyi ndima inotsanangura zvinhu aiziva vanhu vari muchikamu chekudzokera, asi zvakanyorwa zvine hunhu: kunyenganyiso haidzokere kuita "seya" chete nekuda kwekusimama kwenyenganyiso yakanga yakanyanya uye protein inodana nayo, zvakanyatsozara. Mutsara wepanyama wenyenganyiso wakagadziridzwa - zvakawanda zvinonzi "spines", kuita kwezvirimwa zvakasiyana, uye nzvimbo yakasiyana ye"chromatin" kumamiriro akasiyana emagadziridzo - uye kugadziridzwa kwakadaro ndiko kunoratidza nguva refu yekudzoka "kuita sezvairatidzwa." Iyi ndiyowo shoko rakajeka reSections 8 ne10 dziri pazasi.

5. Zvinogadzirisa – Zvinogara Zvakasimba vs. Zvinokwira.

Meseji ese ari muSection 2 anobuditsa kuunganidzwa kweΔFosB kuburikidza nekuyerera kwezviratidzo - kuwanda kwepungwa uye kudonha kwekuita kwezviratidzwa, zvakaitwa

zvakare. "Stabilizers," muchirevo chinoshandiswa pano, ndiwo manereremuro uye zvinhu zvinonyoresa zvinogona kudzivisa iyo pfungwa yekuwanda uye kudonha iyi nekugadzirwa, kana kuti kunobatsira nzvimbo yemakemikari inotungamirira pasina kukanganisa nzira yekubudisa zvakananga. Hapana mumhando dziri muvhidiyo iyi inogona kusunungura kuunganidzwa kweΔFosB kwakaitwa, - chinhu chipi nechipi muvhidiyo iyi chinogona kuzviita nekukurumwa. Zvaanogona kuita, zvinoenderana, ndechekudzivisa kuwedzera, kana kuchengetedza masisitimu akatarisana (kuumbwa kwe dopamine/GABA, basa rematombo anobatsirwa ne methylation) kuti asave chigadzirwa chekumanikidzwa panguva yekuchokwadi.

Mishonga yekurapa zvinetso zvekufunga — Chii chinobata neΔFosB pathway, uye chii chinoshanda kwete.

Izvo zvakakosha kuziva kuti zvimwe zvemagadziriro ekurapa ekufungidzira anogona kushandisa nzira dzakafanana nemazviri ari mutsvene yeTeburu re2, uye chokwadi nderokuti pane zvakawanda, kwete ndege dzekuti "hongu" kana "aisiri".

Hurume dzedu.	Nzira imwechete.	ΔFosB Relevance	Mubvunzo.
Mishonga yekudzivirira huchi (kunyanya mishonga yekutanga inobvisa D2, semuenzaniso haloperidori).	Haisi chinhu chinonzi "Section 2", asi kushanda kwenguva refu kweiyo "D2 receptor blockade" kunounza shanduko dzakadai mumuviri we "striatum".	Kuuraya yendiro inogona kukonzera kuumbwa kwezvikirasi zveAP-1 zvakafanana neΔFosB mumusoro wezvimiro zvemuviri, sezvinoratidza mazuva ekutsvakurudza pamakumbo. Izvi zvinobatsira pakukonzera kuumbwa kwekusununguka kwekuita, iyo inenge yakakosha asi inobata zvimiro zvinofanana.	INGAVO.
Mishonga inokonzera kusimudzira (methylphenidate, amphetamine salts).	Maitiro ekushandiswa kwezvinangwa zve DAT/NET seiyo inowanikwa mumutsetse we methamphetamine (Section 2).	Zvinogona kuita kuti zvive zvakakodzera, asi dosi dzinogadzirisa zvinhu (dosu dzakagadzirirwa kushandiswa kwenguva refu, dzinogadzirirwa kushandiswa kamwe chete pazuva) dzinodzivisa kuwanda kwemaitiro akadzika anozivikanwa nekuti anokonzera zvinhu zvinoita. Munguva chaiyewo, ngozi inogona kuve yakaderera zvikuru pane kushandiswa kwezvinodhaka, asi haisi zero.	INOKUJEKA - nzira yekubatanidzwa, hukama husingaenzaniswi.
Kuuraya yekushandisa zvinonyadzisa (methadone, buprenorphine).	Mu-opioid receptor yakawo seye heroin (Ita 2).	Iri ndiyo zvinoreva zvakarehwa nezve "stabilizer" zvine basa rezvekurapa: kuva nehuwandu hwakadzikama hwekupinda mumuviri uye kuva nechokwadi chekuti doro rinopinda mumuviri nguva dzose zvakakosha kuti zvishandise zvinhu zvinonetsa kuita kuti muviri utange kushandisa doro. Iri imwe yezvikuru zvinodaro kuti OAT (opioid agonist therapy) inzira inokurudzwa uye inobva pazvido, inoshandiswa kuti veduze nekugadzirwa kwemishonga, panze pekuti zvinoenderera nekushandiswa kwezvinonetsa.	ZVINOKANWIRA — chikonzero chinobva pazvinhu zvinobudirira, uye zvakaratidzirwa nemitsetse yekurapa.
Benzodiazepines (dzakatorwa	Maitiro ekufungidzira yeGABA-A yakaratidzwa	Kushandiswa kwenguva refu kunogona kuita kuti mumuviri	KUCHENESA.

Hurume dzedu.	Nzira imwechete.	ΔFosB Relevance	Mubvunzo.
nemishonga, kushandiswa kwenguva refu).	seyakaderera kusvika yakaderera muchigaba chechipiri.	uderere uye kuita kuti kuoma kusunungurwa – asi zvakawanda zvekuti izvi zvinobva pakuderera kwezvinhu zvinoshanda pamusoro zvinonzi GABA-A receptors/kutengesa, kupfuura pakukwira kweΔFosB.	
SSRIs / SNRIs	Haisi chinhu cheSection 2 — kunyudza kwe serotonin uye norepinephrine.	Kuuraya yekuderedera kwezvirwere zvekufara inogona kukonzera kuwanda kweΔFosB mune zvakawanda zvekushandisa, asi mune hippocampus uye frontal cortex, kwete nucleus accumbens, mune nzira inofanirwa kutsigira neuroplasticity. Inenge iri padyo ne "yekudzivirira" inogadzirwa nemitambo (Section 12) kupfuura nzira yekushandisa zvinokonzera kurova. Kupera kwezvirwere zvekufara kunogona kuita, asi nekuda kwezviratidzo zvema receptor asiri ekuti ΔFosB mune nucleus accumbens.	EMERGING (kutangira); ESTABLISHED (kurapwa kunowanikwa, nzira yakasiyana).

Hapana zviri zvinoita kuti urambe kutora mishonga yekurapa zvakakosha, uye iyi haisi hanya yekurapa. Mishonga yakaita seantipsychotics, mishonga inonyadza, opioid agonist therapy, benzodiazepines, uye antidepressants inonetsa, uye inogona kuita matambudziko akakomba, kunyangwa pasina ΔFosB. Chero shanduko yemishonga yekurapa inofanirwa kuitwa nevhakadzi vedzidzo vanovadzidzisa, zvakafanana nemaitiro ekumisa kunwa doro kana benzodiazepines, kunoonekwa sechinongedzo chekurapa, kwete chinhu chekufunga.

Mubatsiro.

Hazvo zvinhu mitatu pazasi haisati dzanyatsoongororwa zvakananga pamusoro peΔFosB. Dzese dzine basa rakanyorwa zvakazvimiririra munzvimbo yemakemikari inogara inoshandiswa nemubvunzo uyu - mukugadzirwa kwe dopamine/GABA, uye kuva nechokwadi kweMTHFR/MAOA cofactor (Section 6, Tier 4) - asi hazvionekwe kuti dziyambise ΔFosB.

Mutoriro.	Chinzvimbo chakagadzirirwa.	Plausible Link to ΔFosB
P5P (Pyridoxal-5'-Phosphate — vitamini B6 inoshanda).	Inzvimbo inodiwa yekuita basa kweAADC (inoshandura L-DOPA ku dopamine, uye 5-HTP ku serotonin) uye glutamate decarboxylase (inoshanda kuita GABA). Kusimba kweB6 kunokanganisa zvakanyanya kuita basa kwekuita dopamine neGABA.	Kugona kwehunhu hwakawanda hwekuita biosynthesis ye-dopamine kunogona, zvakawanda, kuchinja huwandu hwe"signal" inenge ichienda kuD1/PKA/CREB cascade iyo inotanga transcription yeFOSB (Section 6, Tier 3) - izvo zviri kuenzaniswa nemamiriro akakodzera ebiochemistry, asi hazvionekwe zvakananga. [INOKWANISA KUITA, inenge ichienda]
R5P (Riboflavin-5'-Phosphate — B2 inonyanya / FMN)	Cofactor yenzvimbo dzekudya dzine flavoprotein, kusanganisira MTHFR (inonyanya kufungira kune vanhu vane C677T, uyo enzyme yavo inonyanya kuteerera temberature uye inoda FAD) uye MAOA.	Maitiro ekaita: ΔFosB inyanya inoshanda, riboflavin inogona kukanganisa kuti MTHFR ne MAOA dziwane zvakanaka, uye iyo maDNA ayo anenge ane hanya, asi haisati yasimbiswa, kune ΔFosB (Section 6, Tier

Mutoriro.	Chinzvimbo chakagadzirirwa.	Plausible Link to ΔFosB
		4). [INOKUDZIDZIRA, inenge isina chinhu chakajairwa].
Calcium Glycinate.	Inopa glycine (inotarisikirisi yakananga uye inodiwa kuti receptor yeNMDA iita basa rayo). Kupinda kwechairemu kuburikidzo dzeNMDA uye channels dzemagadzirirwo kunobata CaMKII.	CaMKII inzvimbo yakarurama kubva ku CK2, iyo inenge ichiita kuti ΔFosB iwane fosfate, kunyanya paSer27 (Section 1), uye inoshanda nguva dzese, kwete chete panguva yekudzoka kwecha calcium. Hakuna zvinongedzo zvinogadzirwa zvine simba zvinobata zvakanyanya nezve kuchengetedzwa kweΔFosB. [HAKABVUMIRWA].

Maitirose: zvinhu izvi zvinobatsira basa rekemikari remuropa, pasinei nekuti munhu ari papi mu"ΔFosB timeline" inoratidzwa muSection 3. Izvi haisati zvakaratidza kuti zvinoita kuti "timeline" iyi iende, asi nekuti dopamine, GABA, uye enzyme systems inogadzirwa nekuenzanisa zvinhu zviri zvakakosha, kunyange pasina nhau yekushandisa chinhu chinonakidza.

6. Genetics uye Kuchengetedzwa — Mhando Nhatu dzezvinokudzidza.

Genetiki yekubviswa kweΔFosB inogoverwa mumatrini mana, kubva kunemhungwaroti yakasimba kusvika kune yakaderera. Zvakakosha kuti chirevo chiri mumatrini api, nekuti mhungwaroti yakasimba nderemutiro iwe unenge usina kana mumwe munhu ane zvakanyanya, uye hapana bvunzo yemashoko inonyanganyara. Asi, ma jeni aunogona kutestwa kwawo anenge akajairika, asi anenge asiri padyo nemaitiro.

Tier 1 — Kuchinja kwakananga, kuchinja kweFOSB pachayo.

Iyi ndiyo nharo yakasimba zvikuru munharau dzese, uye inobva pakutumira DNA nemudziwo kuenda mumuviri wechipfuyo, zvakanyorwa zvakananga mumweyo wechipfuyo we"nucleus accumbens" - kwete kubva kuzvakaitika zvazvo mumunhu.

Sarudzo.	Zvinoreva here.	Kugadzirisa.	Mubvunzo.
FOSB Ser27Ala (S27A)	Shanduko yechinhu ichinja serine kuva alanine panzvimbo yechikomu 27 — CK2 haigone kuita phosphorylation ku alanine.	Inodzivirira phosphorylation yekuoma zvachose; mune zvidzidzo zvemavector emhando dzemamiriro, apo iyi mutant inoteverwa ku nucleus accumbens, kuenzwa kweΔFosB kunowedzera zvakanyanya uye kuita kwekutadza kwekuita zvinhu kwenguva refu kunogadziriswa.	AKAMBIRWA (chidzira, akagadzirwa).
FOSB Ser27Glu (S27E) — phosphomimetic.	Chinja serine neglutamic acid, zvakaita kuti protein iite seine charge yakaoma, semuenzaniso, seiyo yainge yaita kana yaisvitswa nephosphate. Izvi zvinoreva kuti protein inenge yakasvitswa nephosphate nguva dzese.	Inogadzira chimiro chakagara chakagadzirwa pasina kuda CK2. Inochengeta kugara kwakadaro uye inoratidza mhedzisiro inogara.	AKAMBIRWA (chidzira, akagadzirwa).
FOSB exon-4/intron-4 splice-site variants.	Deredza huwandu hwe PCBP1/SMAD3 hunobatsira kusungirirwa kwemamiriro	Shifts inoratidza kuita kuti kuumbwa kweFosB iende kumusoro, uye kuti FosB yese,	INGAVO.

Sarudzo.	Zvinoreva here.	Kugadzirisa.	Mubvunzo.
	akasiyana.	isina kusvibiswa, iumbwe. FosB iyi inogara kwenguva pfupi. Saka, FosB isina kusvibiswa, isiyo yakanaka, haisumbisi.	

Tier 2 — Magadziridzo anobva kunzvimbo dzakasiyana uye anogadzirisa.

Madziro aya anogadzira maenzimai uye mapuroteni ekuita basa kwekuenzanisa, ayo anoshanda paΔFosB. Kusiyana kwevanhu kwezvemwedzi iri, zvinogona kuva zvakakosha, asi hazvanyatsoongororwa nekubvumirwa kweΔFosB mune vanhu - chete zvakafungwa kubva mumararamiro.

Jeni.	Chinzvimbo.	Kugadzirisa.	Mubvunzo.
CSNK2A1 / CSNK2B (zvimiro zve catalytic uye regulatory zve CK2).	Encode iyo kinase inopokera ΔFosB paSer27.	Kuderera kwechinangwa cheCK2 kunonetsa ΔFosB, ichidzitsvitsa mumamiriro ayo asina phosphorylation, ayo anenge ari ari ari nyore kuurawa - zvichinetsa kuti urwire nekukurumidza.	Zvichiri zvakanganisika (chido, nyeredzi).
PCBP1 / SMAD3	Bhurai rekufambisa chiitiko chekuvandudza kwekusungirira kweDNA kunoita kuti ipe ΔFosB.	Zvakatadza-kushanda zvinogona kusunungurwa zvakanyanya, zvichikonzeresa kuti transcript iwedzere kuita FosB yese, uye kuderedza huwandu hweΔFosB inogara ichiitwa.	Zvikonzeresa zvinogona: * Muchero, zvinhu zvinoshanda.
ACVR1B (ALK4 receptor)	Receptor inogona kuita basa rekubatan SMAD3/PCBP1 splicing complex, inogona kushanda nekuda kwe dopamine D1 signaling.	Kuderera kwe signal inobvisa kuenzwa kwekutendeuka kuenda kuΔFosB — chinhu chinotanga mubhanji rimwechete.	KUCHENESA (chidzisi, michinjeri)

Tier 3 — Magadziridzo eGenes eSystem yeNeurotransmitter.

Iyi data inzvimbo dzekugadzirwa zvemajiini emunhu - asi matanho akaitwa nemazuva akayerera akayera kushandiswa kwezvinodhaka, ngozi yekudzoka, kana kuti mavara emakatekolamini, asi kwete ΔFosB pachayo. Kunyudza kuenda kuna ΔFosB pachake kunogona kuva pfungwa inogona kuita, inobatanidzwa nemamwe data, asi haisi chigadzirwa chakanyorwa zvakananga. Verenga "kunyudza kunotaurwa" nemufaro wekushungurudzwa:

Jeni / Shanduko	Chinzvimbo.	Kune hukama hwakambotaurwa neΔFosB.	Usheuchidzane - Verenga Nemano.
DRD1 (receptor ye dopamine D1) polymorphism.	D1 signaling inotungamirira cascade yekutsvaga maDNA (transcriptional cascade) yePKA/CREB iyo inotanga kutsvaga maDNA kweFOSB.	Zvinhu zvine simba rakakura zvinenge zvichiratidza kuti zvinogona kuwedzera simba remutauro wegene, zvichitungamira kuti zvinhu zvakawanda zviwedzere uye zviyane.	ZVINOKWANISA - logika inogona kuve yakaitika, asi isingafanirwe kuongororwa zvakananga neiyi huwandu hweΔFosB mumunhu.
CHRNB2 rs2072661	Vakwidziridzo ye3' UTR	Kwaitiswa kuti tishandise	INOKUKWANISA -

Jeni / Shanduko	Chinzvimbo.	Kune hukama hwakambotaurwa neΔFosB.	Usheuchidzane - Verenga Nemano.
	mumutauro wejeni remushonga weakanyorwa, inowanikwa muzvidzidzo zvevanhu uye inobatanidzwa nekunetsa kwekutarisira kune nicotine uye ngozi yekudzoka kune zvaaitwa.	mamwe maitiro ekudzikisa basa rematombo akaringana nematombo echolinergic, izvo zvinogona kukanganisa kuumbwa kweΔFosB.	zvakaratidzwa mune zvakanyorwa zvekurapa vanhu kuti zvakayera kuvhunduka uye ngozi yekudzoka kune zvinodhaka, asi kwete ΔFosB pachayo; kubatana kweΔFosB inzira yekufunga, kwete kuyera.
DBH rs1541333	Shanduko mumudzimba we dopamine beta-hydroxylase, inova dopamine ku norepinephrine.	Kuurirwa kushandura zvakakosha zvedopamine uye norepinephrine mumamiriro ekubatsira, uchishandura chinhu chinodiwa kuti ΔFosB iwedzere.	EMERGING — zvakakosha kuti chidzidzo ichi yakayera zvinhu zvinonzi catecholamine uye zvekushandiswa, asi isiri zvakaitwa neΔFosB.

Tier 4 — Pane rekutsvakurudza DNA remabhizinesi akakosha.

Idzi ndegeji dzinogona kuratidzwa nemutsetse weDNA wevashandisi chaiye (data yakakosha seye 23andMe, kana iyo panel inofanirwa mune imwe nzvimbo yecompendium yeRecovery Kernel). Hazviri padyo nechigadzirwa – zviri kure, dzimwe nguva kaviri, kubva pachinhu chine simba paΔFosB.

Jeni.	Zvaanoreva chaizvo.	Link kuΔFosB Clearance.
COMT	Inogadzirisa dopamine ne norepinephrine, zvakanyanya mu prefrontal cortex. Val/Val = kugadziriswa kwakadzika; Met/Met = kugadziriswa kwakadiki.	Haisina data chaiyo. Kunenge kune hukama hwakanga usina kuenzwa zvakananga, asi kungava kuburikidza nekuyerera kwe dopamine. [RUZIVO RWEVAKARWI/SYSTEM]
MTHFR	Inogadzirisa metabolism yefolate uye kugona kwekuita methylation muropa rwese.	Haisina kudyidza hukama hwekusarudzwa kweΔFosB. [HAKABVUMIRWA].
OPRM1 (A118G)	Inogadzirisa huwandu hwekutarisana kwezvinangwa ne-opioid receptor.	Pamusoro zvakananga kwehuwandu hwehutano hunobata opioid; haisvigiwi nekuderera kweΔFosB. [INOKUKWIRA].
GABRA2	GABA-A receptor subunit; inogona kushandiswa kutarisira ngoho yekutambika doro.	Chikuru chinogona kuchangobva kunyika inogona kuita kuti dopamine ishandiswe zvisina kunyarara. [INOKUKIRA]
FAAH (C385A)	Inogadzirisa anandamide; allele yeA inokonzera kuwanda kwe endocannabinoid.	Mubikowo wekudaro inogona kuita kuti munhu ave nemufaro wekudaro weine wezvinodhaka. [INOKWANISA KUITA.]
MAOA	Inokanganisa dopamine, serotonin, uye norepinephrine.	Mubikowo wekunguva inogona kuita musimboti, zvichienzaniswa nekukwira kwezvinonzi monoamines. [RUZWISWA/TSITSI DZECHITUNGO]

Jeni.	Zvaanoreva chaizvo.	Link kuΔFosB Clearance.
SLC6A4 (5-HTTLPR)	Jeni re-serotonin transporter; inongedzwa nezvakawanda zvekuratidzo seine hukama nekugadzirira kwemamiriro ekutya.	Hapana hutano hunobatanidza gene iyi nekuyanduka kweΔFosB. [HAKABATANIDZWA].
ALDH2	Inogadzirisa acetaldehyde inobva pakubura kwemwaka; iyo fomu isina kushanda inogona kukonzera kushushurwa.	Inokanganisa maitiro ekudya uye kunwa, asi kwete ΔFosB pachayo. [RUZWISWA NEVAKURU/SYSTEM, zvakajairika.]
CYP2D6, CYP3A4, CYP2C19, CYP1A2, CYP2C9, CYP2B6	Enzimu dzinogona kuchenesa michiroyidzwa inobva muchimedu uye ichibvisa kubva murwizi.	Ongotarisa kuti chinhu ichocho chinobuda mumuviri nekufamba kwenguva, asi kuti ΔFosB inobuda mune utano nekufamba kwenguva. [RUZIVO/ZVINOGONA ZVECHIZVO, zvakajairika].
HNMT	Inogadzirisa histamine.	Hapana nzira inoratidza kuti inogona kusunungura ΔFosB kana kuti kushanda mumamiriro ekubatsira. [HAKABVUMIRWA].

Hazvo dzinenge dzichidikanwa kuti mumwe munhu achitora nguva yenguva yakawanda kuti ΔFosB yake iende zvachose, hazviwanikwe nemitsetse yezvidzidzo zvekutengesa. Asi, izvozvi ndizvo zviri kuita, asi hazvirevi kuti hazvigone kuita zvinhu zvakawanda. Dhizaini yekubatanidza kuongorora zvakanyanya kweFOSB uye zvinogona kuzoshanduka zvimwe (CK2, PCBP1, SMAD3, ACVR1B), data yese yemararamiro ematombo, uye kuongorora zviratidzo zvakawanda munguva refu apo munhu ari kubva kushandisa chinhu, inogona, mune mamwe mamamiriro, kuita kuti timu yekutsvagura iwane zano rakakodzera kune mumwe munhu. Haisati yabudiswa kana yakasimbiswa nemitsetse yezvidzidzo zvekutengesa — inoda masisitimu akawanda ekuyedza. Kushanda pamwe uye kushandisa maitiro ekutarisa kwenguva refu, kwete seti imwe chete. Izvi ndicho chikonzero chekushaikwa kwezvemari uye yekutsvaga, kwete mutemo wezvinhu. Munhu ane zvigadzirwa zvinofanira, mari, uye kuvengwa, anogona kuita.

7. Kutsvakurudza DNA uye Kugadzirisa Zvakaitika Mune DNA – Zvaunogona Kuwana Zvazvo Nhasi.

Standard Genotyping (SNP Arrays)

Kudhirowa kweDNA kwevanhu, senge iyo inoshandiswa nemamiriro ekushandisa 23andMe, inoverenga nzvimbo dzakagadzirirwa dzinonzi "single-nucleotide" dziri muDNA yevanhu – kusanganisira mageni eTier 3 neTier 4 akaratidzwa pamusoro. Iyi nzira haisi yekuongorora zvakadzika kuti ive nevaraidzo dzinonzi "rare" kana dzinonzi "novel," uye haikwanisi kuona "mutations" dzakagadzirwa dzinonzi Tier 1, dzisiri dzinowanikwa zvakanyanya muvanhu. Iyi nzira inobatsira kune mageni ayo anoverwa, asi haisati yakagadzirirwa kuzvimiririra mubvunzo iri.

Whole-Genome Bisulfite Sequencing (WGBS)

[INOKUJE] sezvakanyorwa panongwaro iyi.

WGBS ndiyo nzira yekushandisa michina yekutarisa DNA, inogona kuongorora kuenzanisa kweDNA - iyo inonzi "epigenetic marking" - pamusoro peDNA yese, panze pekutarisa chete zvikamu zvekugadzirwa kweDNA. Zvido zvekushandisa michina yekutarisa DNA zvakanyanya (izvo kazhinji zvinonzi "WGBS 30x," zvinoreva kushandiswa kwezvakanyanya zvekuongorora DNA, zvakangoita 30) zvinogona kupa sarudzo yakanyanya uye inogutsa yekutarisa

kuenzanisa kweDNA. Sequencing.com parizvino inopa chigadzirwa cheWGBS-30x seimwe yemhinduro dzine mutengo mudiki wekuti munhu ane zvakanyanya anogone kuwana ruzivo rwekuenzanisa kweDNA yese, panze pekushandisa zvikoro zvekurapa zvakagadzirirwa kuongorora DNA.

Zvinogona kukubatsira: Mhando dzekumutsa (methylation) ndidzo dzakakosha muchidikanwa kwe "epigenetic clock" (kusimbisa hutano hwevhu kana kuti hure hwemwoyo kubva mudhina remwedzi). Kushandiswa kwezvinodhaka kwenguva refu kunowanzoita kuti mhando dzekumutsa dzichinje, uye izvi zvinogona kuonekwa muchidikanwa chinobva mudhina remwedzi. Zvinogona kukubatsira here: Hazvisi zvakakosha, uye hazvanyorwe zviri pachigadziriso, kuti pane biomarker inogona kuongorora shanduko dzakaitwa neΔFosB-specific chromatin, sezvakanyorwa Muchigadziriro che4. Shanduko iyi inoitika mumatombo ematombo e"nucleus accumbens", uye matombo aya haafaniri kuongororwa mumunhu ari mupenyana. WGBS (Whole Genome Bisulfite Sequencing) inogona kukubatsira kuti uone mhando dzekumutsa dziri mumatombo ako, asi izvi hazvitenge kuti... kudaro kweΔFosB pachako, pasinei nekuti data iri nyore sei.

WGBS inofungira kuti inzvo inobatsira munhu anoda kuwana data yemusoro wekuita kuti ave nechokwadi nezvemuviri wake mune ramangwana. Uku ndimo imwe yemaitiro akaderera ekutora data yakadaro. Asi, usatarise kuti ripoti ranhasi richakupa nhamba yekuti "mwedzi angangovepi kusvikira ΔFosB yako icharamba". Iri "layer" yekushandisa data yakadaro haisati yabva, kwega kwega, nemutengo wese.

8. Kushandiswa Kwechinhu Chechipfeko Cheshanduko Nenguva Inonetsa Kudaruka Kuzuva.

[RUZIVO/ZVIKIRIRI ZVEMUSHANDISI NEZVECHITINHO] nemidziyo inotsigira uye data yezvinhu zvinobudirira.

Vanhu vanovaka kubva pakushandisa zvinodhaka zvakawanda vanoramba vachitaura kuti kuvaka kwavo kunenge kwakadiki uye kwakaoma kupfuura vamwe vese mukati memaitiro eRecovery Kernel — uye pane chikonzero chinogona kuvakwa pamakemikari anomiririra chikonzero chinowanikwa zvakajeka mune zvakaitwa zvakawanda.

- Convergent induction. Zvese zvakawanda zvemuitafura yepamusoro zvinoita kuti ΔFosB iwedzere nekuda kweiyo nzira imwechete yekupinda – signal ye dopamine inopinda mu nucleus accumbens – kunyange zvazvo zvinoenda neiyo receptor dzakasiyana (kubatwa kweDAT, kutungamirwa kwe-mu-opioid, kuwedzera kwe-GABA-A, nezvimwe). Kushandisa zvimwe zveizvi panguva imwechete hakusi kuita zvinongedzo zvakasiyana, asi kunyudza zvinongedzo imwechete kubva maminagiro akawanda panguva imwechete, zvinoita kuti iwedzere nekukurumidza uye nekunonakira kupfuura zvaizotora kana kushandiswa kweimwe zvinhu chete.
- Stacked chromatin remodeling. Zvinhu zvakasiyana hazvifaniri kukwira kuenzvimbo dzakafanana dzekugadzirwa kwezviratidzo zvegene pasi peΔFosB. Zvinodhaka, opioids, uye doro dzine zviratidzo zvayo zvekugadzirwa kwezviratidzo zvegene zvakanyorwa mumabhuku nezvekururama. Kushandisa zvinodhaka zvakawanda kunogona kutungamirira kumapato akawanda ekuchinja kwechromatin (Section 4) kuenzvimbo dzakawanda zvegene uye maderivhi, izvo zvinoreva kuti pane nguva yakawanda yechinhu chinofanira kugadziriswa, kwete kungowedzera huwandu hwechinhu chimwechete.
- Zvinhu zvakanyorwa nezve kugadzirisa zvakaratidzwa. Pasina zvakakosha nezve nzira dzinobva mumatomu, kushandiswa kwezvinodhaka zvakawanda kunowanzoitika kuti kupera kwemanoita zvakanaka, kuwanda kwezvinangwa, uye kupera kwezvinodhaka zvakanyanya kupfuura kushandiswa kwezvinodhaka chimwe chete, zvakadaro

zvinoratidzwa mune zvinyorwa zvevarapi. Iri basa rinogara panzvimbo yakasimba kupfuura nzira dzinonyanya kushandiswa neΔFosB — ndeimwe yezvinhu zvakaratidzwa zvakajairwa, pasinei nekuti chii chakakosha nezve nzira dzinobva mumatomu.

Hapana zviri izvi zvinoreva kuti kudzokera kubudiriro kubva pakushandisa zvinodhaka zvakawanda hakusi chinhu chekufunga. Dhizaini yeRecovery Kernel yakagadzirirwa zvakanyanya kuti ibatsire vanhu vane matambudziko akakura. Zvinoreva kuti, nguva dzinofanirwa kushandiswa pakudzokera kubudiriro dzinofanirwa kuongororwa semhangura, asi kwete semigumisiro, kune vanhu vanenge vashandisa zvinodhaka zvakawanda.

9. Chidzidzo - Trinity yeKemisikisi (Meth, Cathinones, GHB)

"Chemsex" - kushandiswa kwezvidonge, kazhinji methamphetamine, cathinone se mephedrone ("cat"), uye GHB/GBL, dzimwe nguva ne MDMA kana ketamine - kazhinji inenge yakanyanya kuoma kudzika, zvakaurwa nevanoshandisa uye nevabatsiri. Chidzidzo chemakemikari muchigadzirwa chinoongorora chikuru chemhando yekuti nei zvakaita, asi hazviongorore zvese.

Mishonga.	ΔFosB Induction (kubva muSection 2)	Basa remurume wechipiri muTriini.
Methamphetamine	Zvakakwirira zvikuru.	Iyo simbi inonyanya kukonzera kushanda kwe dopamine mu zvinhu zvakabatanidzwa - kufamba kwe DAT/NET kunobva kunounza kushanda kwe dopamine zvakananga, kwete kungoderedza kuuya kwayo.
Mephedrone / cathinones ("cat")	High.	Hupfura hupfura hupfura

Mishonga.	ΔFosB Induction (kubva muSection 2)	Basa remurume wechipiri muTriini.
		hupfura hupfura hupfura

pamwe chete; pane zvikuru zvinoratidza kuti zvinowedzera simba remumwe nemumwe pane iyo nzira yemakemikari.

- Sesheni dzepamweduro dzinobvisa chinhu chimwe chete chinoshanda sechinzvimbo yekudzivirira, chinhu ichi chiri kufemerwa zvakawanda muchimiro ichi. Sesheni dzechimwe chinhu chinonzi "chemsex" dzinowanzogara kwemaminitsi akawanda kusvika kumazuva, nekuwedzera kwezvinonzi "redosing" uye nekunzeva kwemwedzi shomanje. Uye, chikamu che12 chakaratidza kuti kusina mwedzi shomanje kunogona kuita kuti zvinhu zvisvike zvakanaka. Muchimiro, izvi zvinenge zviri kuenzaniswa nemamiriro ekukonzera ngozi akawanda akataurwa muchimiro chacho, zvinenge zvichidikanwa panguva imwechete, zvakare zvakare.

GHB/GBL inenge inengo dambudziko rakakosha risiri rinobva paΔFosB: kushandiswa kazhinji kungaita kuti uive nemhosva mwedzi shomwe, uye kupera kwezvinangwa kunoitwa nehutano hunhuwaira hweGABA, kungaita sekuti kwaariro uye benzodiazepines. Inogona kukonzera kusavhunduka, kurova, uye matambudziko akanyanya anogona kureva kuti anoda kurapwa kwakanyanya. Kurega kushandisa GHB/GBL kazhinji uye pasina kutarisirwa nemukozi wehutano zvinenge ngozvizhinji. Iri ndiyo rudzi nderubayiro rakakosha rakatanga bhuku rekuti "kuvara" - verengai zvine uchenjeri.

Nezviito: Zvakaratidzwa mune zvinyorwa zvekurapa kuti kushandiswa kwe-methamphetamine kunowanzoitwa nevanhu vanoshandisa kemikisi kunoratidza kuti vanenge vane utsinye hwakakura hwekurwadziwa mwoyo, kushungurudzika, PTSD, uye psychosis, iko kunenge kuchidikanika kana kushandiswa kwacho kuchidikanika. Zvakadaro, zvakaratidzwa kuti kushandiswa kweGHB/GBL kunowanzoita kuti vanhu vasarudze kuenda kunoona vaenzi, uye kushandiswa kwakadaro kunenge kuchikatidza kuti vanenge vasarudza kuenda kunoona vaenzi. Izvi zvinonzwisiswa, asi hazvifanirwe kupinzwa zvizhinji, neΔFosB.

10. "Zuva Rekudzima" Zvakatove, "Kudzoka Kumusoro," uye Nei Kudzoka Kune Zvinhu Zvinenge Zvakatove.

Iri rimwe remigwagwa yakakosha zvikuru muchimiro chino, nekuti inotsanangura chinhu chaive nechokwadi kuti vanhu vazhinji vanenge vachipedza nekuderedza zvinangwa avo vachiona: kusunungurwa zvakazvo — "kusunungurwa kwekutengesa," "mwedzi wekusunungurwa," "kuedza kudzosa zvinhu kuita senge zvakanga zviri," uye nekubva kuderedza zvinangwa zvacho, uye kushandiswa kwacho kunobva kudonha zvakasimba zvikuru, kunenge kudzoka kuita senge kwainge kwava panguva yega. Kwakadzoka, nekukurumwa, senge pasina nguva yakapfuura.

[INGANGOZI] (yakaitwa nemaitiro akavakwa muSection 4, uye yakashandiswa pakudzorerwa - nzira yakazivikanisa muchidzidzo chekuvapo kwezvirwere mumhuka).

Heano inotanga, zvakanyanya: kudzoka kunobva kunobvumira protein inonzi ΔFosB kuti idonse – chikamu ichi chekudzoka chakakwana, uye chikamu ichi chikaitwa nechiedza che3 chinotsanangura. Asi chikamu che4 chakataura chinhu chinoramba pachiyitwa neprotein apo ichienda: chromatin yakagadziridzwa panzvimbo dzakasiyana dzejiini (yakadzvanyidzwa pa c-fos ne HDAC1, yakatengeswa pa CDK5/GluA2/ARC ne BRG1), uye kuwedzera kwemamiriro ezvinhu emadendritic spine panenzvimbo dze neurons dziri mu circuit yekubatsira. Hazvionepi chinhu ichi zvakare panguva imwechete neprotein. Circuit haidzokeri kuve nemamiriro ayaitenge zvakare panguva yekutanga kwe addiction nekuda kwe ΔFosB. zvakazvazvimirira — iri circuit yakarongwa, asi iri mumamiriro ekutyiwa nguva pfupi.

Kana kushandisa chinhu chinoshandiswa zvakare, hazvichengete ΔFosB munzira itsva sezvakaita panguva yekutanga. Inochengeta ΔFosB munzira iyo yatova nematombo, receptor,

uye chromatin yakagadzirirwa kubva pakare. Kukudziridza ΔFosB inogara zvakanyanya munzira yakagadzirirwa zvakare kunotora nguva shoma kupfuura kukudziridza yekutanga, nekuti basa rakawanda rekukudziridza zvakanyanya rakaitwa. Izvi zvinoshanda neparadigm yekushandiswa kwezvinodhaka yekudzidzisa zvakanyanya kuita kuti zvinhu zvikwaniswe zvakare, uko Kudzorora kamwe chete mushure mekuyambura kunobva kudzosa kufunga nezvekudonha zvinhu zvakanyanya nekukurumidza kupfuura nguva yacho yakatanga kuita – uye ndeiyi ndiyo shoko rakanyatsogadzikana remamiriro ezvinhu emabviro anowanzoita vanhu vachiti, "Ndiri kuenda nekudzoka kuita, pakarepo, nemhepo imwechete, uye handikwanisi kutsigira kuti nei zvakazodonha zvakanyanya nekukurumidza."

Izvo zvakakosha nderokuti, hazvirevi kuti kudzima kunenge kusina musimboti - nguva yekudzima inoramba ichiine musimboti, uye chero kupfupisa kwenguva yacho kunowedzera, inzvo zvakanaka chaizvo. Izvo zvakakosha nderokuti, kudzima hakafanire kurongwa kana kuvimbiswa sekuvharidzwa zvachose. Muviri unogara achiri nezvakawanda zvaanonzwa, uye kushandisa zvakare pashure pekudzima kunenge kunenge kunoshanduka mune zvakawanda kupfuura kutanga zvachose.

11. Kurutidzira kwezvinhu mumisodzi uye kurutidzira kwehutano hwehutano.

[INOKUJEKA] (mifananidzo yemhando dzemhuka; nzvimbo itsva uye isina kuvandudzwa zvakadzika senyika dzeSections 1–4)

ΔFosB inoratidza basa risiri kungwarira nezve kushanduka, asiwo nezve kufamba kwemwoyo uye mabviro ekushungurudzika. Sechikamu checomplex yeAP-1 (inobatanidzwa zvakanyanya naJunD), inoshanda mumamiriro anobatanidzwa nekuderera kwemwoyo - mamiriro acho mwoyo unoramba kushandira uye anogadzirwa nemamiriro akasiyana, ayo anowanzo kuva nemoto.

- Muneuroteni, anogona kushanduka, kunyenganyiswa kwenguva refu kana kutonhora kwakanyanya kunogona kuzvitsa mumamiriro akafanana anozivikanwa se stress-induced premature senescence (SIPS). Kushanda kweΔFosB kwenguva refu, pamwe nechinhu chinofanana (EGR3), kunobva kuzvikonzeresa kuwanda kwezviratidzo zveDNA-damage-response (GADD45B/G) uye p21 (CDKN1A), izvo mumamiriro aya anogona kukanganisa synaptic plasticity uye kudzikisa hippocampal neurogenesis.
- Mune masero asiri nematombo — astrocytes uye microglia — kuiswa kwenguva refu kweAP-1 kunowanzoitwa neSenescence-Associated Secretory Phenotype (SASP): masero ematombo akura anogadzira michepa inonyudza kurutidzika, iyo inogona kusarudza kurutidzika pasi-pasi kumatombo akavakira. Kuwanda kwehormone yekushungurudzika kwechinguva (CRF, glucocorticoids) kunogonawo kuwedzera zvinhu izvi.
- Kusiyana-siyana, uye mamiriro ezvinhu nemugero wemuviri anokosha. Muchikafu chehypothalamus, kuwanda kweΔFosB kunowanzoitika nekugona kwakanaka kweiyo metabolism munguva yekukura kwezvimweni (kukwanisa zvakanaka kweglucose, kudzikiswa kwekuvapo kwehuwandu hwezvimweni). Mukuongororwa kwemamiriro akasiyana-siyana ekutonhora uye Alzheimer's, kuwanda kweΔFosB muchikafu chehippocampus kunoratidza kuti kunogona kudzivisa kufa kwemasero nekuda kwekusimba kwakanyanya, kunyange zvazvo kunogona kukanganisa zvimwe zvekugadzirisa zvekufunga. Iyi ndiyo nzira yekubatsira, kwete kuipa chete.

Iyi basa iri inofanirwa kuwedzerwa kuti zvive zvakakwana, uye nekuti iri nzvimbo inogara ichidikanidzwa mukutsvakurudza kweiyo molecule imwechete - asi kwete nekuti ichichinja cheroipi chinhu muzvinyorwa zvepamusoro zvine chekuita nekudzorerwa. Iyi ndiyo basa nyowani, isina kuvandudzwa zvakakwana, apo isu takatanga kutsvakurudza nezve

kushandiswa kweiyi molecule, kusiyana neiyo nzvimbo yekushandiswa kweiyi molecule yekurapa kushanduka, iyo iripo muzvinyorwa zvemupfungwa 1 ne4.

12. Zvaanobatsira Chaizvo - Inotsigirwa Nemanyorerwo Akafanana.

- Kusimuka zvakawanda - chinhu chikuru, uye chinhu chete chinodzorera zvinhu zvakaderera nekukurumidza kupfuura nekugadzirwa kwazvo.

[AKATONGO] Kufamba zvakanyanya zvine hanya kunounzawo shanduko muΔFosB mu nucleus accumbens — nekugadzirisa kwakasiyana neiyi zvinonetsa, uye inowanikwa mune zvimwe zvirongwa nemhuka sekuvengwa uye kuderedza kutsvaga chinhu, panzvimbo peiyo nzira isina kunaka. Iprotein yacho, inounzwa nenzira yakasiyana, inogona kushandira kupokana nechirwere panzvimbo yekubatsira.

- Kurapwa - kuchengetedzwa kwezviratidzo kunoreva kufungidzira kuti kunoda kurapwa zvakakwana; kushoma kwekurapwa kwenguva refu kunogona kuita kuti zvinhu zvisave zvakanaka.
- Kuderera kwemamiriro ekutya - Kuderera kwemamiriro ekutya, pachake, kunounza kuwanda kweΔFosB nekuda kweHPA axis, uye kunowedzera kuwanda kweΔFosB kunoita zvinogona kuita kuti munhu adare.
- Nguva, zvinhu zvisiri nyore - nhanho yekuramba zvinhu uye kushandisa zvikuru, inogona kutora masvondo kusvika kumwedzi, kwete masikati. Kutarisira kuti nguva yezvose ichiri mavhiki maviri kunogona kuita kuti zvinhu zvikanganise kana zvinhu zvakawanda zvakaitika, uye izvi zvinogona kukonzera kuti uende kumusoro zvakare nekuda kwezvikonzerero zvehutano hwemuviri - uye sezvakaurwa muSection 10, kushandisa zvakare panguva iyoyo kunoreva kuti unenge watanga zvakare, asi haisi kutanga zvakare kubva pakutanga.

Chidzidzo ichi yakapedzwa.

ΔFosB inotsanangura, nenzira yechisayenzi, kuti nei zvakajairika zvinogona kudzokorora kuita, kunyange apo zvikonzerwa zvekurega zvakajeka zviri pachena — uye kuti nei kurega, kunyange kana kwakakwana, hakusi zvakafanana nekudzoka kumazuva akareba. Haisi yese nhau, uye panguva iyoyo haigone kuongororwa zvakanyatsosarudzwa mumunhu ari mupenyu, uye hapana bvunzo iri pamusika nhasi inogona kukubata zuva rekurega kwako. Shandisa zviri nyore, sekuti iyo framework yese yeRecovery Kernel inokumbira kuti ushandise chidiki chimwe chete chebhayoloji — semamiriro akatendeseka, anogadzirika, muenzaniso wakakura, asi. seka uchitarisa.

Zvekufunda zvinoenderana nemubvunzo uyu: Maitiro Ekudzoka Kubva Kune Alcohol, Maitiro Ekudzoka Kubva Kune Cocaine, Maitiro Ekudzoka Kubva Kune Crack Cocaine, uye Bhuku Rakazara ReProtocols (Bhuku re3 - Zvido Zvekufamba uye Mhinduro Dzinopesa, uye Bhuku re1 - Kukwira Mhosva uye Nhaka Yemwoyo).